

## **REMARKS**

In the Action, the examiner variously rejected claims 1-16 under 35 U.S.C. §112, first paragraph as assertedly lacking enablement, and under 35 U.S.C. §103(a) as assertedly obvious in view of Cherukuri et al., U.S. Patent 6,344,222 (hereinafter “Cherukuri”), in view of McCullough et al., U.S. Patent 6,495,605 (hereinafter “McCullough”), further in view Eswara, U.S. Patent 5,780,051 (hereinafter “Eswara”) and Hanauer, S., Gut 51:182-83, 2002 (hereinafter “Hanauer”). Reconsideration is requested in view of the amendments and remarks made herein.

### **I. Election of the Invention**

Applicant confirms that in a telephone discussion with the examiner dated August 13, 2007, Applicant elected to pursue Group I, methods of treating ulcerative colitis, claims 1-16, and further elected for examination on the merits: (1) nicotine, as the species of nicotine compound, (2) bupropion as the species of anti-depressant, and (3) budesonide as the species of additional ulcerative colitis treatment.

### **II. Amendment to the specification**

The specification has been amended to properly indicate use of trademarks where appropriate. The amendment includes no new matter.

### **III. Support for the amendment to the claims**

Support for amendment to the claims can be found throughout the specification. The claims have been amended to cancel claims to a non-elected invention and to eliminate reference to some non-elected species.

Claims 2 and 8-13 have been canceled. Applicant reserves the right to pursue any cancelled subject matter in a duly filed continuing application.

Claim 1 has been amended to incorporate the subject matter of claim 2. Claim 14 has been amended to correct claim dependency after cancellation of claims. The amendment includes no new matter.

**IV. The Rejection of Claims 1-16 Under 35 U.S.C. 112, Enablement, Should Be Withdrawn**

The examiner rejected claims 1-16 under 35 U.S.C. §112, first paragraph, as directed to subject matter allegedly lacking enablement, asserting that, while the specification is enabling for administration of a composition comprising nicotine and bupropion, the specification does not enable use of any nicotine analog or nicotine antagonist and any anti-depressant.

Applicant has amended the claims solely to expedite prosecution and not for reasons of patentability. The claims as amended are directed to administration of a composition comprising nicotine and bupropion, thereby obviating the examiner's rejection.

**V. The Rejection of Claims 1-16 Under 35 U.S.C. §103(a) as Assertedly Obvious Should Be Withdrawn**

The examiner rejected claims 1-16 under 35 U.S.C. §103(a) as being directed to subject matter allegedly rendered obvious in view of Cherukuri and McCullough, as evidenced by Eswara, and further in view of Hanauer. The examiner asserted that a worker of ordinary skill in the art would have been motivated to combine the anti-smoking compounds described in Cherukuri and McCullough with the ulcerative colitis treatments described in Hanauer to arrive at the present invention. The examiner asserted that because each of the publications above disclose an element of the invention claimed herein, *e.g.*, nicotine (Cherukuri), bupropion (McCullough) and budesonide (Hanauer), and because Eswara teaches that bupropion is a substitute for nicotine, it would be obvious to one of ordinary skill to combine these elements to arrive at the present invention. Applicant respectfully disagrees.

The claims as amended are directed to a method of treating ulcerative colitis comprising administering composition comprising nicotine in combination with bupropion. The treatment may optionally include use of an existing ulcerative colitis treatment, such as the corticosteroid budesonide.

Cherukuri teaches use of a chewing gum delivery system as a smoking cessation therapy. Cherukuri neither discloses nor suggests use of nicotine to treat ulcerative colitis, nor suggests a pharmaceutical composition comprising nicotine and bupropion for the treatment of colitis. McCullough describes compositions comprising bupropion for the treatment of smoking

cessation. McCullough neither discloses nor suggests use of bupropion to treat ulcerative colitis, nor suggests a pharmaceutical composition comprising nicotine and bupropion for the treatment of colitis. Hanauer teaches that budesonide is a compound for treating ulcerative colitis. Hanauer neither discloses nor suggests use of nicotine in combination with bupropion to treat ulcerative colitis.

Eswara describes methods and compositions for treating nicotine withdrawal symptoms and promoting smoking cessation. Eswara teaches that bupropion is a sensory altering nicotine substitute, and defines a "sensory altering nicotine substitute" as a compound which when administered to a subject alters the subjects sensory perception such that the subjects awareness of nicotine withdrawal is reduced (col. 4, lines 59-62). Eswara differentiates sensory nicotine substitutes from receptor binding nicotine substitutes, which are agents that actually bind the nicotinic receptor (col. 3, lines 49-53). Thus, bupropion is not a "substitute" for nicotine in a chemical sense as the examiner seems to be implying, but is a psychological substitute for the gratifying effect of nicotine on the patient suffering from nicotine withdrawal. Therefore, bupropion could not substitute for nicotine in the treatment of ulcerative colitis on a chemical level. Additionally, bupropion, though effective in smoking cessation due to its an anti-depressant quality, would not be expected to have a similar effect as on a patient suffering from ulcerative colitis, and would not be a likely therapeutic for ulcerative colitis due to the physical symptoms of the illness rather than psychological symptoms. As such, the examiner's inference that Eswara evidences that bupropion could "substitute" for nicotine in the treatment of ulcerative colitis is misplaced.

To establish a *prima facie* case of obviousness, the examiner must show that all the elements of the claim are taught or suggested in the prior art (MPEP 2143.03 and Federal Register Examination Guidelines for Determining Obviousness, Section III.A.1, Fed Reg., Vol 72, No. 195, 2007). Further, to establish obviousness, if prior art elements are described in the art, the combination of elements must yield predictable results to render a claimed invention obvious. Neither Cherukuri nor McCullough disclose the disorder ulcerative colitis, and certainly do not suggest that either nicotine, bupropion, or both compounds together, are useful to treat a disease associated with inflammation of the intestinal tract. Hanauer discloses administration of the corticosteroid budesonide and other anti-inflammatory drugs to treat ulcerative colitis, but does not teach treating colitis with nicotine or bupropion, or a combination

of the two compounds. As such, all the elements of the claimed invention are not taught in the cited art.

In addition, based on the disclosure in the art, the combination of elements to treat colitis would not lead to predictable results. Studies in ulcerative colitis patients had shown some positive effect of nicotine on ulcerative colitis, but the results were often patient dependent and produced unwanted side effects (see page 2, lines 18-29 of the specification), while bupropion demonstrates some negative side effects with respect to bowel irritation (Croft *et al.*, Clin Ther. 1999, 21(4):643-58) (abstract submitted herewith). Additionally, none of the cited references or general knowledge in the art discussed administration of nicotine in conjunction with bupropion to treat ulcerative colitis. Although some elements of the present invention may have been described individually in the art, the elements would not have been predictably combined by one of ordinary skill in the art in order to arrive at the subject matter of the invention.

Additionally, to establish obviousness, it should be demonstrated that the prior art reference(s) provide a teaching, suggestion or motivation to combine the references, and/or there is a reasonable expectation of success (MPEP 2142 and Federal Register Examination Guidelines for Determining Obviousness, Section III.G, Fed Reg., Vol 72, No. 195, 2007). As stated above, nicotine has been shown to have some benefit to ulcerative colitis patients, but the results were patient dependent (see page 2, lines 18-29 of the specification), and it was known that bupropion can lead to increased diarrhea and bowel irritation (Croft *et al.*, Clin Ther. 1999, 21(4):643-58). Thus, none of the cited references or general knowledge in the art discussed or suggested administration of nicotine in conjunction with bupropion to treat ulcerative colitis. Cherukuri, McCullough and Hanauer do not remedy the deficiencies since the references provide no additional guidance on the treatment of colitis using the methods of the invention. As such, the combination would not reasonably be expected to be a beneficial treatment in ulcerative colitis because it was unknown from the prior art whether any clinically relevant, therapeutic benefit would result from the administration of nicotine and bupropion to treat ulcerative colitis. Therefore, one of ordinary skill would have no reasonable expectation at arriving at the present invention based on the knowledge in the art and the cited references.

Further, one of ordinary skill in the art reading Cherukuri and McCullough, both of

which teach use of a nicotine or bupropion, respectively, to assist in smoking cessation, would not be motivated to look to Hanauer which discusses treatment of ulcerative colitis using completely different compounds, such as corticosteroids and other anti-inflammatory compounds. A person of ordinary skill in the art of treating smoking cessation and nicotine addiction would not be motivated to look at the disclosure of Hanauer, which describes methods of treating a disease relating to inflammatory bowel disease using corticosteroids, to find an additional anti-smoking compound because the three references are not analogous, that is, smoking cessation and colitis treatment are wholly dissimilar conditions. Likewise, one of ordinary skill in the art reading Hanauer and searching for a new treatment for colitis would be motivated to review disclosure related to anti-inflammatory compounds, and not disclosures related to anti-smoking therapies. Therefore, the art cited by the examiner provides no motivation to one of ordinary skill to arrive at the present invention.

For the reasons above, the rejection of claims 1-16 under 35 U.S.C. §103(a) as obvious over Cherukuri and McCullough in view of Eswara further in view of Hanauer should be withdrawn.

## **VI. Conclusion**

Applicant submits that the application is in condition for allowance and respectfully requests notice of the same.

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Respectfully submitted,

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